

LISTING OF THE CLAIMS

Claim 1 (canceled)

Claim 2 (currently amended) A method according to claim 1 for the production of a single heavy chain antibody in a non-human mammal comprising expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus comprises:

(a) at least one VHH region each comprising one VHH exon, at least one D region each comprising one D exon and at least one J region each comprising one J exon, wherein the VHH exonregion, the D exonregion and the J exonregion are capable of recombining to form VDJ coding sequence,

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells and

which locus when expressed leads to the formation of a single heavy chain antibody said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claim 3 (canceled)

Claim 4 (currently amended) A method according to claim 3 for the production of

a single heavy chain antibody in a non-human mammal comprising expressing a camelised VH heavy chain locus in that mammal specifically in B cells in response to antigen challenge
wherein the camelised VH heavy chain locus comprises:

(a) at least one VH region each comprising one VH exon which is mutated such that, when expressed, the resulting single heavy chain antibody is stabilised, at least one D region each comprising one D exon and at least one J-region comprising one J exon, wherein the VH exonregion, the D exonregion and the J exonregion are capable of recombining to form VDJ coding sequence, and

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

and which locus when expressed leads to the formation of a single heavy chain antibody said method comprising:

1) immunizing said mammal with an antigen and

2) isolating single heavy chain antibody against said antigen from said mammal.

Claims 5 – 6 (canceled)

Claim 7 (currently amended) A method according to claim 1 or 2 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exonregion of human origin and at least one J exonregion of human origin and a constant region of human origin.

Claim 8 (currently amended) A method according to claim 3-~~or~~ 4 wherein the camelised VH heavy chain locus comprises at least one D exonregion of human origin and at least one J exonregion of human origin and a constant region of human origin.

Claim 9 (canceled)

Claim 10 (currently amended) A method according to claim 1-~~or~~3 2 or 4 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 (original) A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 (canceled)

Claims 17 - 32 (canceled)

Claim 33 (currently amended) The method of claim 1-~~or~~ 2 wherein the entire VHH single heavy chain locus is of camelid origin

Claim 34 (currently amended) The method of claim 3-~~or~~ 4 wherein the camelised VH single heavy chain locus is of human origin.

Claim 35 (currently amended) The method of claim 3-~~or~~ 4 wherein the camelised VH single heavy chain locus is of non-human origin.

Claim 36 (currently amended) The method of claim 3-~~or~~ 4 wherein the camelised VH single heavy chain locus is of camelid origin.

Claims 37-38 (canceled)

Claim 39 (new) The method according to claim 2 or 4 wherein the non-human

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mammal is a rodent.

Claim 40 (new) The method according to claim 2 or 4 wherein the regulatory sequence is a locus control region.